REMARKS

Reconsideration of the application and following remarks is respectfully requested. Claims 2 through 63, and 197 through 199 are pending in this application.

New Claim

Claim 199 has been added which specifically claims a biomaterial having an integrated catalyst or catalyst precursor as a biomaterial of the invention. Support can be found on page 17 of the application wherein the definition of "modification" includes an integrated catalyst or catalyst precursor.[1] No new matter has been added.

Rejections under 35 U.S.C. § 103(a)

In the Office Action, claims 2-63, 197 and 198 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ragheb *et al.* (U.S. Patent No. 6,774,278) in view of Malfroy-Camine *et al.* (U.S. Patent No. 5,696,109) and Shastri *et al.* (U.S. Patent No. 5,837,752). Specifically, the Office Action asserts that Ragheb *et al.* discloses:

> "a coated implantable medical device wherein Ragheb outlines a wide range of bioactive materials that may be employed including free radical scavengers and antioxidants. Ragheb *et al.* is silent to the particular species of the genus of free radical scavengers and antioxidants."

The Office Action also asserts that Malfroy-Camine *et al.* discloses:

> "a synthetic catalytic free radical scavenger useful as antioxidants for prevention and therapy of disease. The catalyst is a non proteinaceous material having manganese and iron chelates compounds. To provide the specific free radical scavenger catalysts of Malfroy-Camine *et al.* with a biomaterial substrate or carrier of Ragheb *et al.* to effectively reduce the available free radicals at the tissue site of the medical device would have been obvious to one with ordinary skill in the art base on selection of a known species of the broad genus of bioactive materials."

In addition, the Office Action states that Shastri *et al.* discloses:

> "various biopolymers, including hyaluronic acid, fibrin, collagen and saccharides, and ceramics, including hydroxyapatite, that

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1 Page 17 of the application: "modification" means any method by which a physical association may be effected between a biomaterial and a non-proteinaceous catalyst for the dismutation of superoxide, whereby the non-proteinaceous catalyst becomes integrated into or onto the biomaterial.

> may be used in the manufacture of medical devices. Ragheb *et al.* discloses general base materials that are used in the fabrication of the medical device. To use hyaluronic acid as a base material for the medical device would have been obvious to one with ordinary skill in the art based on substitution of equivalent elements."

Applicants respectfully traverse this rejection. Applicants submit that the Office Action has failed to state a *prima facie* case of obviousness. The burden of proof in establishing a *prima facie* case of obviousness under §103 rests with the Patent Office. *In re Piasecki*, 745 F.2d 1468, 1472 (Fed. Cir.1984). In establishing a *prima facie* case, the Patent Office, among other things, must show that (1) the prior art would have suggested to those of ordinary skill in the art that they should make the claimed invention and (2) that the prior art would have revealed a reasonable expectation of success. *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1999). In addition, the prior art reference (or references when combined) must teach or suggest all the claim limitations. "Both the suggestion and the reasonable expectation of success must be found in the prior art, not in the applicant's disclosure." *Id.*; *see also* MPEP § 2143. Thus, "particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed." *In re Kotzab*, 217 F.3d 1365, 1371 (Fed. Cir. 2000). "[T]he factual inquiry whether to combine references must be thorough and searching. It must be based on objective evidence of record. This precedent has been reinforced in myriad decisions, and cannot be dispensed with." *In re Lee*, 277 F.3d 1338, 1343 (Fed. Cir. 2002) (citations omitted).

The present Office Action fails to provide objective evidence of ***any*** suggestion or motivation in the prior art to combine and modify the cited references. Instead, the Office Action merely states that such combinations and modifications "would have been obvious." It is now well-established that "[b]road conclusory statements regarding the teaching of multiple references standing alone are not 'evidence'." *In re Dembiczak*, 175 F.3d 994, 999 (Fed. Cir. 1999); *see also In re Kotzab*, 217 F.3d at 1370. "Th[e] factual question of motivation is material to patentability, and [can]not be resolved on subjective belief and unknown authority." *In re Lee*, 277 F.3d at 1343-1344. Because the Office Action fails to provide any objective evidence from the prior art of a motivation to modify and combine the cited references along with a reasonable expectation of success, Applicants respectfully submit that the Office Action fails to state a *prima facie* case of obviousness but rather relies upon hindsight in combining the various

disparate references in contravention of the Federal Circuit's ruling in *Sensonics, Inc. v. Aerosonic Corp.*, 81 F.3d 1566 (Fed. Cir. 1996).

Additionally, Applicants respectfully submit that the Office has failed in its burden to show that when the invention is considered ***as a whole*** and the references are considered ***as a whole***, as required by law, that the prior art references teach or suggest all the claim limitations of Applicants' invention. There is a clear contrast between the references cited against the present application, either alone or in combination, and the present invention which, taken as a whole, discloses a modified biomaterial, where "modification" means there is physical association effected between the biomaterial and catalyst or precursor ligand, whereby it becomes ***integrated into or onto*** the biomaterial[2].

In contrast, Ragheb *et al.* discloses nothing more than a medical device "that provides a controlled ***release*** of an agent, drug or bioactive material..." *See* col.3, ll 14-15 and variously throughout. Ragheb *et al.* refer to the term "release" no less than forty-five times to describe the mode in which that medical device operates. That reference does not provide any teaching of a catalyst or precursor ligand being effective while integrated into or onto a biomaterial. Thus, when Ragheb *et al.* is taken ***as a whole***, that reference only teaches the use of a compound to be released from the medical device. Ragheb *et al.* teaches away from Applicants' invention, which requires a catalyst or catalyst precursor to be integrated into or onto a biomaterial, and therefore does not suggest or motivate the present invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). In addition, Shastri *et al.* do not teach or suggest the use of a non-proteinaceous catalyst for the dismutation of superoxide integrated into or onto a biomaterial for catalytic dismutation of superoxide anions.

As provided previously, Malfroy-Camine simply teaches administering the salen-metal antioxidants to a subject in free form. Therefore, that reference does not teach one skilled in the art how to make or use a catalyst or precursor ligand integrated a biomaterial. Accordingly, Malfroy-Camine does not disclose a catalyst or precursor ligand integrated into or onto a biomaterial substantially compatible with a biological system as required by each claim. Because it is not possible to simply extrapolate the free form antioxidant features of this reference to the catalyst integrated a biomaterial of the present invention, the Malfroy-Camine

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2 See footnote 1.

reference is not analogous art that enables the practice of Applicants' claimed invention under either 35 U.S.C. §103(a).

With respect to Shastri *et al.*, the Office Action asserts that:

> "various biopolymers, including hyaluronic acid, fibrin, collagen and saccharides, and ceramics, including hydroxyapatite ... may be used in the manufacture of medical devices. "

This assertion also fails to consider the reference of Shastri *et al.* as a whole. The compositions disclosed in Shastri *et al.* are polymerized using "any suitable free-radical initiators," *i.e.*, any free radical ***producers***. Col. 9, ll. 10-19 and ll. 60-67. The Office Action fails to consider, however, that the present application involves a catalyst or precursor ligand integrated into or onto a biomaterial capable of dismutating superoxide, *i.e.*, free radical ***scavengers***. Thus, Shastri *et al.* is not analogous art which can properly be cited against the present application where there can be no expectation of successful integration of free radical scavengers of the present invention into or onto the polymers requiring free radical producers of Shastri *et al.* In addition, Shastri *et al.* do not teach or suggest the use of a non-proteinaceous catalyst for the dismutation of superoxide integrated into or onto a biomaterial for catalytic dismutation of superoxide anions.

"A prior art reference must be considered in its entirety, *i.e.*, as a whole, including portions that would lead away from the claimed invention." *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). The same assertion also impermissibly distills the invention down to a "gist" or a "thrust" and disregards the "as a whole" requirement. *See* 35 U.S.C. §103 and MPEP §2124.02. "Distilling an invention down to the "gist" or "thrust" of an invention disregards the requirement of analyzing the subject matter "as a whole." *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). As stated in the application:

> "Prior to applicants' invention, it was not known that non-proteinaceous catalysts for the dismutation of superoxide could be immobilized on the surface of a biomaterial ***and still retain their catalytic function*** and exhibit an anti-inflammatory effect."

Page 25, ll. 16-24.

In addition, there is no motivation or suggestion within the references to combine Ragheb *et al.* with either Malfroy-Camine *et al.* or Shastri *et al.* or the combination of the three references. There is no reasonable expectation of success if the references are combined, as

Ragheb *et al.*, Malfroy-Camine *et al.*, and Shastri *et al.*, each taken as a whole, teach away from Applicants invention.

> "It is impermissible to use the claimed invention as an instruction manual or 'template' to piece together the teachings of the prior art so that the claimed invention is rendered obvious. This court has previously stated that '[o]ne cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.'

In re Fritch, 972 F.2d 1260, 23 U.S.P.Q.2d 1780 (Fed. Cir. 1992).

Applicants respectfully submit that the current rejection functions exactly in the manner the court in *In re Fritch* warns against. The rejections impermissibly cite different features of the claimed invention from prior art sources without the motivation or suggestion in the art to modify the references. "[The] Examiner must prove that it would have been obvious to modify the references, without having access to the application under examination to arrive at the claimed invention." *Lear Siegler, Inc. v. Aeroquip Corp.*, 733 F.2d 881, 221 USPQ 1025, 1033 (Fed. Cir. 1984).

CONCLUSION

For the foregoing reasons, prompt reconsideration and allowance of claims 2-63 and 197 through 199 is respectfully requested. Applicants believe that there is a fee of $1,020.00 due at this time for a three month extension to reply to the Office Action. Any deficiency or overpayment may be charged or reimbursed to Deposit Account No. 19-3140.

Respectfully submitted,

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